

- c. sequencing said nucleic acid to yield a newly-identified sequence;
- d. adding said newly-identified sequence to said initial pool to generate a second complex subtraction probe pool, said second pool comprising a larger number of labeled probes compared to said initial pool;
- e. contacting a second ordered array of nucleic acid samples from said population with said second subtraction probe pool; and
- f. repeating steps b.-e., wherein each repeat of steps b.-e. reduces the redundancy of said population of nucleic acid molecules, thereby enhancing the rate of novel gene discovery.

59. The method of claim 58, wherein said redundant or known sequence is selected from the group consisting of a public database member gene, a housekeeping gene or ribosomal gene.

60. The method of claim 58, wherein said first and said second ordered array comprise DNA immobilized on a glass surface.

61. The method of claim 58, comprising repeating steps b.-e. to generate a Unigene set.

62. The method of claim 58, wherein said weak hybridization comprises a signal-to-noise ration of less than 0.5.